## Remarks

Claims 8-13 are pending in the current application.

## Rejections under 35 U.S.C. §103

Claims 8-13 are rejected under 35 U.S.C.§103(a) as being unpatentable over Gaubitz et al. (1993) ("Gaubitz") in view of U.S. 6,228,363 and Madaio et al. (1996). It is alleged to be obvious to combine the teachings of the '363 patent, which discloses that R38 is derived from laminin and is recognized by lupus antibodies (Madaio also discloses that laminin is recognized by lupus antibodies) with the teachings of Gaubitz, which describes immunoadsorption of a subject's plasma for removal of pathogenic antibodies.

Applicant respectfully traverses this rejection and incorporates by reference all previous arguments presented in the most recent response, particularly in regard to the assertion by the Examiner that evidence of unexpected results must properly appear in the specification of the application as filed. As recently as December 2008, in Sanofi-Synthelabo v. Apotex, Inc., the Federal Circuit permitted the patentee to present evidence of nonobviousness at trial in a challenge to the validity of a patent under §103.

Applicant submits herewith, in the Supplemental Information Disclosure Statement, an article entitled "Removal of Pathogenic Auto-antibodies by Immunoadsorption". This article provides specific support for the proposition that one skilled in the art cannot determine, *a priori*, if methods of **treatment** using extracorporeal immunoadsorption to remove specific autoantibodies will successfully treat the disease. As set forth in this article at page 639, first full paragraph, the authors note that in the treatment of myasthenia gravis, attempts at selective removal of one class of autoantibodies, those specific to the alpha-67-76 sequence (the alpha subunit) of the Ach receptor protein were unsuccessful, due to the low affinity of peptides containing this sequence to the autoantibodies, even

when conformation changes were introduced in the peptides to improve their antigenicity. The following paragraph goes on to state that "the specificity of the technique, which is its major advantage, proved to be a significant drawback because the anti-AChR blocking antibody is merely one subpopulation among several others implicated in the pathogenesis of MG."

Thus, given 1) the small size of the R38 protein, 2) possible changes in conformation due to binding on a substrate, 3) possible differences in antibody-antigen affinity of the R38-antiR38 antibody combination as compared to the sheep antibody/Fc system of Therasorb™, 4) the very low level of anti-R38 antibodies in plasma, and 5) the plasma flow rate required to make this method of treatment viable, one cannot say that successful treatment is reasonably expected.

Applicant submits that in view of the above comments, the differences between the invention and the prior art, and the evidence of unexpected results, any so-called *prima* facie case of obviousness has been overcome. Withdrawal of the §103 rejection is respectfully requested.

**Conclusion**

Applicant submits that all outstanding issues have been addressed and that Claims 8-13 are in condition for allowance; such action is respectfully requested at an early date.

Respectfully submitted,

Edward Langer
Reg. No. 30,564

c/o Shiboleth, Yisraeli, Roberts, Zisman & Co.
1 Penn Plaza – Suite 2527
New York, NY 10119
Telephone (212) 244-4111
Fax (212) 563-7108